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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Application No.	Applicant(s)
09/593,629	CAMERON ET AL
Examiner	**Art Unit**
Bharati R. Dhruva	1632

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1☐ Certified copies of the priority documents have been received.

2☐ Certified copies of the priority documents have been received in Application No. _____

3☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18)☐ Interview Summary (PTO-413) Paper No(s). _____
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other

DETAILED ACTION

Objection

Claim 16 is objected to because of the following informalities: Claim 16 recites. "The method according to claim 17."which is improper dependence. It should read "The method according to claim 15."

There are minor errors in the specification; for example page 8 line 5, "cryopreserved pig Sertoli cells" should be "cryopreserved pig islet cells". Applicants should check for additional errors and correct them.

Appropriate correction is required.

Objection

The disclosure is objected to because of the following informalities:

References at the end of the specification (pp.22-24) are incomplete. Applicants must supply the full citation or delete the references.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-8 are towards a biological chamber system and claims 9-12 are to a transplantation facilitator comprising a biological chamber system. It is not clear what is meant by biological chamber system. There are no method steps describing the formation of the chamber, the outer wall and the inner lumen. The claims further recite engineered Sertoli cells but the claims do not set forth any steps involved in the engineering of the Sertoli cells. The claims do not define what is an engineered cell. Does it mean that the cells are genetically altered? The specification does not disclose how the cells are altered.

Claim 13 does to make sense. What does "about the therapeutic cells" means and also what does" re-engineering" refer to?

Claim 24 has improper Markush language. The claim recite "group consisting essentially or" which is not correct. It should be "the group consisting of ".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a biological chamber system comprising sertoli cell construct forming a center lumen surrounding a population of cells which are different than the sertoli cells. The claims are further drawn to a transplantation facilitator comprising a biochamber, a method of making a biochamber, a method of transplanting cells comprising a biochamber consisting of facilitator cells and therapeutic cells. The claims are further drawn to the method of transplanting cells comprising forming a biochamber and incorporating therapeutic cells into biochamber and transplanting the biochamber into a host. Hence the only disclosed use of the invention is for a therapeutic outcome.

The specification describes cocultivation of sertoli cells and islet cells (pp. 17, lines 20-28) and teaches formation of sertoli-neuron aggregated cells (pp. 19, lines 1-18 and Fig.6) when grown in high aspect rotation velocity bioreactor (HARV) and Matrigel. Furthermore, the specification discloses that after *in vitro* exposure to glucose, the sertoli-islet cell biochambers produced insulin and the presence of sertoli cells enhanced the insulin secretion. The specification also describes that some of the NT2 cells in neuronal-sertoli biochambers expressed tyrosine hydroxylase, indicating dopamine synthesis (pp.20 lines 7-10).

The specification does not describe or teach *in vivo* transplantation and insulin synthesis by the islet-sertoli biochambers or *in vivo* transplantation and dopamine synthesis by NT2-sertoli biochambers. Furthermore the specification is silent on how many biochambers or how large a biochambers has to be implanted to achieve the therapeutic outcome, what is the amount of protein needed for the therapeutic outcome,

how long the biochambers would be actively producing the therapeutic proteins, and how often the biochambers would be transplanted.

The specification cites prior art, which taught immunoprotection of the grafted islet cells and maintenance of normoglycemia in diabetic rat by co-transplantation of the islet cells with sorteli cells. The specification does not teach *in vivo* implantation of the biochambers, production of therapeutic proteins and therapeutic outcome.

Additionally, the specification does not define what are the facilitator cells beside the sertoli cells and fails to teach if any and all cells could form the center lumen containing biochambers. Furthermore the specification does not teach the isolation procedure, growth conditions, growth media and condition, use of HARV or Matrigel, for formation of the biochamber and transplantation vessel for any other type of cells but sertoli cells. It is well known in the art that different cell types have different growth conditions; for example Hela cells do not need any additional growth factors but those supplied by fetal bovine serum while muscle cells, CRL-1999, in addition to fetal bovine serum need insulin, ascorbic acid and transferrin (On line ATCC catalog) while for myotube formation from primary mouse skeletal muscle cells grown on matrigel require addition of FGF,PDGF, TGF $_{\beta 1}$ (Maley et al. Experimental Research, 219, 169-179).

Furthermore, the specification fails to address if the facilitator cells produced from other cells than the sertoli cells are capable of immunoprotecting the therapeutic cells and secreting therapeutic products produced by the therapeutic cells.

In view of the lack of guidance provided in the specification for the implementation of the invention as claimed with regard to the *in vivo* transplantation and

therapeutic protein production using the islet-sertoli cell or NT2cell-sertoli cell biochambers, the observation that *in vitro* NT2-sertoli biochamber had only few NT2 cells producing tyrosine hydroxylase, lack of *in vivo* working example of biochamber, lack of teaching in the prior art for making biochambers comprising any two types of cells, the growth conditions for cells other than the sertoli cells, lack of teaching on the formation of biochambers with other type of cells but sertoli cells, lack of guidance for using biochambers made with other types of cells, lack of teaching for *in vivo* transplantation of the biochambers, and the wide breadth of the claim, it would require an undue amount of experimentation for one of skill in the art to implement the invention as claimed. There is no disclosed use of the invention but for transplantation of biochambers and therapeutic outcome due to transplantation. The specification as discuss above does not teach transplantation of biochambers or achieve therapeutic outcome.

Thus no claims are allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Bharati R. Dhruva whose telephone number is (703) - 605-1157. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Schwartzman can be reached on (703) 308-7307. The fax phone

numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and for After Final communications.

Question of formal matters can be directed to the patent analyst Phillips Williams, whose phone number is (703) 305-3482.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)-308-0196.

BRD

June 26, 2001

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER